

CLAIMS

1. A method for obtaining a cell model, wherein said model comprises a set of expression vectors that confer to the transformed cells a phenotypic profile of drug biotransformation enzymes comprising:

5 (a) transforming cells expressing cytochrome reductase with at least one expression vector,

wherein each expression vector comprises a DNA sequence that codes for a different drug biotransformation enzyme, selected from:

(i) a DNA sequence transcribed in the sense mRNA of a drug biotransformation enzyme; and

(ii) a DNA sequence transcribed in the anti-sense mRNA of a drug biotransformation enzyme;

wherein the expression of said DNA sequence in the cells transformed with at least one expression vector confers on the transformed cells a specific phenotypic profile of a drug biotransformation enzyme, and

15 (b) obtaining cells that transiently express said DNA sequence and present a different phenotypic profile of drug biotransformation enzymes.

2. The method of claim 1, wherein said cells are selected from human or animal cells.

20 3. The method of claim 2, where in said cells are tumour cells.

25 4. The method of claim 1, wherein said cells are human cells selected from cells of hepatic, epithelial, endothelial and gastrointestinal type CaCO-2 cells.

5. The method of claim 1, wherein said drug biotransformation enzymes are selected from oxygenases, oxidases, hydrolases and conjugation enzymes.

6. The method of claim 1, wherein said drug biotransformation enzymes are selected from monooxygenases dependent on CYP450, flavin-monooxygenases, sulfo-transferases, cytochrome C reductases, UDP-glucuronyl transferases, epoxide hydrolases and glutathione transferases.

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7. The method of claim 1, wherein said DNA sequence coding for a drug biotransformation enzyme comprises at least one DNA sequence from DNA sequences transcribed in the sense mRNA or anti-sense mRNA of CYP450 isoenzymes and DNA sequences transcribed in the sense mRNA or anti-sense mRNA of oxygenases, oxidases, 10 hydrolases and conjugation enzymes involved in drug biotransformation.

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8. The method of claim 1, wherein said DNA sequence comprises at least one DNA sequence from DNA sequences transcribed in the sense mRNA or anti-sense mRNA of CYP 1A1, CYP 1A2, CYP 2A6, CYP 2B6, CYP 2C8, CYP 2C9, CYP 2C18, 15 CYP 2C19, CYP 2D6, CYP 2E1, CYP 3A4, CYP 3A5, GST(A1), and DNA sequences transcribed in the sense mRNA or anti-sense mRNA of flavin-monooxygenases, sulfo-transferases, cytochrome C reductase, UDP-glucuronyl transferase, epoxide hydrolase or glutathione transferase.

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20 9. The method of claim 1, wherein said DNA sequence is a DNA sequence transcribed in the sense mRNA of a Phase I or Phase II drug biotransformation enzyme.

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10. The method of claim 1, wherein said DNA sequence is a DNA sequence transcribed in the anti-sense mRNA of a Phase I or Phase II drug biotransformation 25 enzyme.

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11. The method of claim 1, wherein said expression vector is selected from viral vectors, liposomes and micellar vehicles.

12. The method of claim 11, wherein said expression vector is chosen from natural and recombinant adenovirus.

13. The method of claim 1, which comprises using variable amounts of at least 5 two said expression vectors comprising DNA sequences coding for the drug biotransformation enzymes selected from Phase I drug biotransformation enzymes and Phase II drug biotransformation enzymes.

14. A method for studying a drug, which comprises placing said drug in 10 contact with a cell model obtained according to the method of claim 1.

15. Use of sense or anti-sense expression vectors of Phase I or Phase II drug biotransformation enzymes in the manipulation of cells expressing cytochrome reductase activity to reproduce the metabolic variability found in humans.

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16. A kit comprised of one or more expression vectors coding for the sense and anti-sense mRNA of the Phase I and Phase II drug biotransformation enzymes.

17. A method to confer to a selected cell line the capacity to metabolize 20 xenobiotics in a controllable manner by means of a set of adenoviral expression vectors of Phase I and Phase II drug biotransformation enzymes and cytochrome P450 reductase, comprising the transfection of said cell line with said adenoviral expression vectors to confer to the transfected cells a pre-selected phenotypic profile .

18. The method of claim 17, wherein the selected cell line expresses cytochrome P450 reductase activity, and the set of expression vectors comprises DNA sequences coding for P450 enzymes involved in xenobiotic biotransformation, wherein each expression vector comprises aDNA sequence transcribing for the sense mRNA of a different CYP enzyme.

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19. The method of claim 17, wherein the set of expression vectors comprises at least one DNA sequence coding for drug biotransformation enzymes selected from Phase I or Phase II drug biotransformation enzymes, wherein each expression vector comprises a DNA sequence transcribing for the sense mRNA of a different Phase I or Phase II drug biotransformation enzyme.

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20. The method of claim 17, wherein the selected cell line contains CYP genes but the cell line does not express CYP reductase and the set of expression vectors comprises DNA sequences coding for at least one of said CYP genes and DNA sequences coding for CYP reductase, wherein each expression vector comprises a DNA sequence transcribing for either the sense mRNA of a CYP enzyme or the sense mRNA of a CYP reductase.

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21. A cell model having a phenotypic profile of at least one drug biotransformation enzyme, comprising:

a cell having cytochrome reductase activity, transformed with at least one expression vector comprising a DNA sequence for a drug biotransformation enzyme.

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22. The model of claim 21 wherein the DNA sequence is chosen from DNA sequences for oxygenases, oxidases, hydrolases, and conjugation enzymes.

23. The model of claim 21 wherein the DNA sequences are chosen from monooxygenases dependent on CYP450, flavin-monooxygenases, sulfo-transferases, cytochrome C reductases, UDP-glucuronyl transferases, epoxide hydrolases and glutathione transferases.

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24. The model of claim 21 wherein the DNA sequences are chosen from CYP 1A1, CYP 1A2, CYP 2A6, CYP 2B6, CYP 2C8, CYP 2C9, CYP 2C18, CYP 2C19, CYP 2D6, CYP 2E1, CYP 3A4, CYP 3A5, and GST(A1).